DETAILED ACTION

1. The amendment filed Dec. 23, 2008, has been entered.

2. Claims 2, 3, 12, 14, 15, 17-19, 24 and 25 have been cancelled.

Claims 1, 4-11, 13, 16, 20-23, and 26 are pending.

Claims 6-10 and 20-23 are withdrawn.

3. Claims 1, 4, 5, 11, 13, 16, and 26 are examined in the present office action.

4. This application contains claims 6-10, and 20-23 drawn to inventions nonelected with traverse in the response filed July 9, 2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. If the elected product claims are amended such that they are allowable, then product claims that depend from or otherwise include the limitation will be rejoined (ie. claims 20-23). Claims 6-10 will not be rejoined and should be cancelled.

Rejections and Objections that are Withdrawn

5. The rejection of claims 1, 2, 4, 5, 11, 13, 16 and 26 under 35 U.S.C. 112, second paragraph, is withdrawn in light of the Applicant's amendment to claim 1 which clarifies the enzymatic activity that is required.

6. The rejection of claims 4 and 5 under 35 USC 112, first paragraph, for lack of written description and enablement is withdrawn.

7. The rejection of claims 1, 2, 4, 11, 13, 16, and 26 under 35 USC 112, 1st paragraph, for lack of scope of enablement is withdrawn in light of the Applicant's amendments to the claims, and in light of their arguments regarding the level of skill in the art and the ability to practice the invention without undue experimentation (see page 10 of the response).

8. All rejections of claim 2 are withdrawn in light of the Applicant's cancellation of claim 2.

Specification

9. The abstract remains objected to because it should specify the gene that has been elected for prosecution; in particular, it should specify that it is the Arabidopsis GalAt1 gene. In the response filed on Dec. 11, 2008, the Applicant amended the abstract to include a reference to SEQ ID NO:1; however, this does not identify the source of the sequence. It is recommended that the Applicant delete the reference to SEQ ID NO:1, and instead include the information that the enzyme was identified in Arabidopsis.

10. The title of the invention remains objected to because the amendment inserts "(GALAT1)" without underlining. When submitting an amendment, new words should be underlined. Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1, 11, 13, 16, and 26 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record stated in the previous Office Action mailed on Aug. 29, 2007, and for the reasons stated below. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Applicant's arguments in the response filed on Feb. 29, 2008, were fully considered but were not found to be persuasive.

The claims are broadly drawn to isolated nucleic acids encoding a polypeptide that comprises a sequence with at least 50% identity to SEQ ID NO:2 and that has galacturonosyltransferase (GALAT1) activity that catalyzes transfer of

galacturonosyl residues to an oligomer of galacturonic acid residues, and to vectors and plants comprising said nucleic acids, including wherein the nucleic acid has at least 90% identity to SEQ ID NO:1.

The essential feature of the nucleic acids of the instant invention is that they encode polypeptides that catalyzes transfer of galacturonosyl residues to an oligomer of galacturonic acid residues (See claim 1).

The Applicants describe the nucleic acid of SEQ ID NO:1 (also referred to as At3g61130) which encodes the polypeptide of SEQ ID NO:2 (see pages 28-29 and the sequence listing). The Applicants describe a bioinformatics search that identified 10 genes with 23-29% sequence identity, and they describe several motifs and conserved residues that are present in these genes (see page 18 and figure 7). The Applicants describe the polypeptide of SEQ ID NO:2 as having galacturonosyltransferase activity (see page 9, lines 24-25 and Figure 8).

The Applicants do not describe any polypeptides having 50% identity to SEQ ID NO:2 other than SEQ ID NO:2, itself, that are known to comprise galacturonosyltransferase activity. Nor do they describe any polypeptides encoded by a nucleic acid having 90% identity to SEQ ID NO:1 (other than SEQ ID NO:2) that are known to have galacturonosyltransferase activity.

The Applicant's have provided evidence in a declaration under 37 CFR 1.132 on Dec. 11, 2008. They have provided evidence that the instant SEQ ID NO:8 (referred to as GAUT6) has galacturonosyltransferase activity. This polypeptide

has 46% identity and 64% similarity at the amino acid level to the instant SEQ ID NO:2 (referred to as GAUT1) (see Table 3 provided in the supporting evidence submitted on Dec. 11, 2008). While this evidence does provide support for at least one other protein that has galacturonosyltransferase activity; this does not provide an adequate description for the subset of the extremely large genus of polypeptides that have 50% identity to SEQ ID NO:2 wherein the subset of polypeptides are capable of transferring galacturonosyl residues to an oligomer of galacturonic acid residues. Reducing two members of this large genus to practice is not sufficient to provide adequate support for the breadth encompassed by the current claims.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F. 3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The Applicants fail to describe a representative number of polypeptides that have GalAT activity and have as little as 50% identity to SEQ ID NO:2 or are encoded by nucleic acids with 90% identity to SEQ ID NO:1, and they fail to describe a representative number of nucleic acids encoding such polypeptides. The

Applicants only describe the polypeptide of SEQ ID NO:2, and one nucleic acid encoding it, SEQ ID NO:1. Furthermore, the Applicants fail to describe structural features common to members of the claimed genus of polypeptides that have GalAT activity. They merely disclose motifs found in a bioinformatics search utilizing amino acid sequences for which there has not been any activity empirically determined. Even though they have provided evidence that one more member of the large family has galacturonosyltransferase activity; this does not provide sufficient support for the extremely large genus being claimed. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for GalAT activity, it remains unclear what features identify polypeptides capable of such activity. Since the genus of polypeptides and nucleic acids encoding such polypeptides has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

SEQ ID NO:2 consists of 673 amino acids. Polypeptides that have as little as 50% identity to SEQ ID NO:2 can have 336 amino acid substitutions within the polypeptide; therefore, this genus of molecules encompasses 20^{336} molecules. Nucleic acids encoding these polypeptides encompass an even larger genus of molecules because of codon redundancy. Nucleic acids with as little at 90% identity to SEQ ID NO:1 can have 202 substitutions because SEQ ID NO:1 is 2022 nucleotides in length. Therefore this genus of nucleic acids encompasses 4^{202}

molecules. Furthermore, if each of those 202 substitutions can cause a change in the amino acid encoded by the particular codon, then the resulting polypeptide can have 202 amino acid substitutions relative to SEQ ID NO:2 which results in a protein having as little as 70% identity to SEQ ID NO:2.

Nucleic acids that encode polypeptides with as little as 50% identity to SEQ ID NO:2 or that have 90% identity to SEQ ID NO:1 encompass multitudes of molecules, many of which would not produce a polypeptide with GalAT activity upon being transcribed in a plant cell, and most of which were not in the possession of the Applicant at the time of filing. The Applicants have only reduced one molecule to practice in an experiment that demonstrates GalAT activity; and one additional molecule in post-filing experiments, as evidenced by the declaration provided on Dec. 11, 2008. Accordingly, the specification fails to provide an adequate written description to support the genus of nucleic acids that encode polypeptides with 50% identity to SEQ ID NO:2 that comprise GalAT activity or that have 90% identity to SEQ ID NO:1 and encode polypeptides that comprise GalAT activity as set forth in the claims. (See Written Description guidelines published in 2008 online at http://www.uspto.gov/web/menu/written.pdf).

The Applicant argues that those of ordinary skill in the art are highly educated and technically sophisticated and that they have taught conserved regions of the protein; they have provided a reference by Sterling et al as a supporting document (see page 10 of the response filed Dec. 11, 2008). The information in the

Sterling reference (published in 2006), can not be relied upon to provide adequate written description, because the written description must be in the application at the time of filing. The Examiner agrees that one of ordinary skill in the art is highly sophisticated. However, the Applicant has argued that proteins with 53.7%, 64.1%, and 90.5% identity to the instant SEQ ID NO:2 do not necessarily comprise the recited galacturonosyltransferase activity (see pages 11-13 of the response filed on Dec. 11, 2008). Therefore, one of skill in the art would need some description of what motifs, domains, or other structural elements are required for galacturonosyltransferase activity to be able to distinguish the subset of polypeptides with at least 50% identity to SEQ ID NO:2 that also have galacturonosyltransferase activity. Because the specification does not provide enough guidance to determine if a protein with 53.7% identity or 64.1% identity or 90.5% identity to SEQ ID NO:2 actually has galacturonosyltransferase activity, then the specification does not provide adequate written description for this large genus of proteins.

It is the Examiner's opinion that there is adequate written description for the genus of nucleic acids encoding an enzyme comprising a polypeptide with at least 95% identity to SEQ ID NO:2, wherein said polypeptide is capable of transferring galacturonosyl residues to an oligomer of galacturonic acid residues.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1, 11, 13, and 16 remain rejected under 35 U.S.C. 102(a) as being anticipated by Harper et al (US 2002/0160378, published on Oct. 31, 2002). The Applicant's arguments in the response filed on Dec. 11, 2008, were fully considered but were not found to be persuasive.

The claims are drawn to isolated nucleic acids encoding a polypeptide having galacturonosyltransferase (GalAT) activity and having 50% similarity with SEQ ID NO:2, and to vectors and plants comprising said nucleic acids.

Harper et al teach a nucleic acid encoding a protein with 53.7% identity to the instant SEQ ID NO:2, and they refer to this nucleic acid as SEQ ID NO:1120 (see sequence alignment). They teach a method of producing a transgenic plant with altered responsiveness to at least one stress condition by introducing the nucleic acid of SEQ ID NO:1120 into the plant (see claim 29) including wherein the nucleic acid is operably linked to a heterologous promoter (see claim 35). They teach transgenic plants and seeds (which are progeny) produced by this method (see claims 42 and 44). Although they are silent with regard to any galacturonosyltransferase activity, the protein encoded by this nucleic acid has

53.7% identity to the instant SEQ ID NO:2, and this is within the claimed identity (see claim 2). Therefore, if 53.7% identity is sufficient for conferring galacturonosyltransferase activity to a protein, then the protein expressed by the method taught by Harper et al would inherently comprise such activity.

The USPTO does not have a laboratory to test for galacturonosyltransferase activity, and therefore, the burden shifts to the Applicant to demonstrate that that the prior art nucleic acid does not anticipate the claimed nucleic acids. Where the prior art product seems to be identical, except that the prior art is silent to a characteristic or property claimed, then the burden shifts to Applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. See *In re Best* 195 USPQ 430, 433 (CCPA 1977).

The Applicant argues that the prior art does not teach any enzymatic activity, let alone the present claimed activity, and that for a proper anticipation rejection, the inherency must be a necessary aspect of the prior disclosure (see page 11 of the response). This is not persuasive, however, because the inherent property does not need to be disclosed in the prior art reference. If the prior art is silent about the inherent property or characteristic; but the prior art product otherwise appears to be the same as the product being claimed, then inherency is appropriate.

It is noted that the Applicants have provided evidence in a declaration under 37 CFR 1.132 on Dec. 11, 2008. They have provided evidence that the instant SEQ ID NO:8 (referred to as GAUT6) has galacturonosyltransferase activity. This

polypeptide has 46% identity and 64% similarity at the amino acid level to the instant SEQ ID NO:2 (referred to as GAUT1) (see Table 3 provided in the supporting evidence submitted on Dec. 11, 2008). Therefore if 46% identity is enough identity to cause galacturonosyltransferase activity, then 53% identity should also be sufficient for having galacturonosyltransferase activity. Because the USPTO does not have laboratory facilities, the burden shifts to the Applicant to provide evidence that the prior art does not have this inherent property.

13. Claims 1, 11, 13, and 16 remain rejected under 35 U.S.C. 102(e) as being anticipated by Liu et al (US 2004/0034888, published on Feb. 19, 2004, and filed on April 28, 2003, with priority to May 6, 1999). The Applicant's arguments in the response filed on Dec. 11, 2008, were fully considered but were not found to be persuasive.

The claims are drawn to isolated nucleic acids encoding a polypeptide having galacturonosyltransferase (GalAT) activity and having 50% similarity with SEQ ID NO:2, and to vectors and plants comprising said nucleic acids.

Liu et al teach a nucleic acid encoding a protein with 64.1% identity to the instant SEQ ID NO:2, and they refer to this nucleic acid as SEQ ID NO: 32781 (see sequence alignment). They teach a method of producing a transgenic plant having an improved property by introducing a construct comprising a promoter operably joined to the nucleic acid of SEQ ID NO: 32781 into the plant (see claim 3). They

teach transgenic plants and offspring produced by this method (see page 8, paragraph 0081). Although they are silent with regard to any galacturonosyltransferase activity, the protein encoded by this nucleic acid has 64.1% identity to the instant SEQ ID NO:2, and this is within the claimed identity (see claim 2). Therefore, if 64.1% identity is sufficient for conferring galacturonosyltransferase activity to a protein, then the protein expressed by the method taught by Harper et al would inherently comprise such activity.

The USPTO does not have a laboratory to test for galacturonosyltransferase activity, and therefore, the burden shifts to the Applicant to demonstrate that that the prior art nucleic acid does not anticipate the claimed nucleic acids. Where the prior art product seems to be identical, except that the prior art is silent to a characteristic or property claimed, then the burden shifts to Applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. See *In re Best* 195 USPQ 430, 433 (CCPA 1977).

The Applicant argues that the prior art does not teach any enzymatic activity, let alone the present claimed activity, and that for a proper anticipation rejection, the inherency must be a necessary aspect of the prior disclosure (see page 11 of the response). This is not persuasive, however, because the inherent property does not need to be disclosed in the prior art reference. If the prior art is silent about the inherent property or characteristic; but the prior art product otherwise appears to be the same as the product being claimed, then inherency is appropriate.

It is noted that the Applicants have provided evidence in a declaration under 37 CFR 1.132 on Dec. 11, 2008. They have provided evidence that the instant SEQ ID NO:8 (referred to as GAUT6) has galacturonosyltransferase activity. This polypeptide has 46% identity and 64% similarity at the amino acid level to the instant SEQ ID NO:2 (referred to as GAUT1) (see Table 3 provided in the supporting evidence submitted on Dec. 11, 2008). Therefore if 46% identity is enough identity to cause galacturonosyltransferase activity, then 64.1% identity should also be sufficient for having galacturonosyltransferase activity. Because the USPTO does not have laboratory facilities, the burden shifts to the Applicant to provide evidence that the prior art does not have this inherent property.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14 Claims 1, 11, 13, and 16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Brummell et al (PMB (2001) Vol. 47, pp. 311-340) in view of Tavares et al (PMB (2000) Vol. 42, pp. 703-717). The Applicant's arguments in the

response filed on Dec. 11, 2008, were fully considered but were not found to be persuasive.

The claims are drawn to isolated nucleic acids encoding a polypeptide having galacturonosyltransferase (GalAT) activity and having 50% similarity with SEQ ID NO:2, and to vectors and plants comprising said nucleic acids.

The instant claims are obvious over the prior art because there had been a recognized need in the art to develop methods to manipulate fruit ripening and plant cell walls, there had been a finite number of identified predictable potential solutions, including manipulating glycosyltransferases in transgenic plants, and one of ordinary skill in the art could have pursued any of the potential options with a reasonable expectation of success at the time of the invention.

Brummell et al teach that cell wall metabolism is important for fruit softening and quality, and this metabolism is carried out by numerous enzymes associated with different modifications to carbohydrates in the cell wall (see entire article). They teach that suppression and over-expression of the enzymes in transgenic plants is preferred over *in vitro* methods for the study of function of the enzymes (see second paragraph in left column on page 312).

They do not teach a nucleic acid encoding a polypeptide with at least 50% identity to SEQ ID NO:2.

Tavares et al teach a nucleic acid encoding a polypeptide with 90.5% identity to SEQ ID NO:2 (see alignment), they refer to this polypeptide as LGT1 and they

identify it as a glycosyltransferase (see paragraph bridging left and right columns on page 704). They teach that it catalyses the transfer of glycosyl groups to a carbohydrate core (see right column on page 704).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to modify the transgenic plants taught by Brummell et al to utilize any of the glycosyltransferases that were commonly known in the art; especially one, such as the LGT1 taught by Tavares that is taught to catalyze the transfer of glycosyl groups to a carbohydrate core. The use of strong constitutive promoters to drive high levels of expression was known in the art at the time of filing, and it would have been obvious to utilize a strong promoter to drive expression of the LGT1 nucleic acid in a transgenic plant. It would have been obvious to produce offspring of such plants. One of ordinary skill would have had an expectation of success in producing such plants, and one would have expected the result would be a change in the carbohydrates and structures in the cell walls of the plants.

Although Tavares et al are silent with regard to any galacturonosyltransferase activity, the protein encoded by this nucleic acid has 90.5% identity to the instant SEQ ID NO:2, and this is within the claimed identity (see claim 2). Therefore, if 90.5% identity is sufficient for conferring galacturonosyltransferase activity to a protein, then the protein expressed by the

method taught by Tavares et al would comprise such activity, and this would naturally flow from the combination of the teachings.

The USPTO does not have a laboratory to test for galacturonosyltransferase activity, and therefore, the burden shifts to the Applicant to demonstrate that that the prior art nucleic acid does not render obvious the claimed nucleic acids. Where the prior art product seems to be identical, except that the prior art is silent to a characteristic or property claimed, then the burden shifts to Applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. See *In re Best* 195 USPQ 430, 433 (CCPA 1977).

The Applicant argues that Tavares references to proteins "like glycosyltransferases" and that there are myriad glycosyltransferases in plants, and there is nothing in the cited references which would have led the skilled artisan to the particular nucleic acid molecules and encoded polypeptides which are claimed (see third paragraph on page 13 of the response). This is not persuasive, however, because Tavares et al specifically teach that the LGT proteins catalyze the transfer of clygosyl groups to a carbohydrate core (see top of right column on page 704). Therefore, they have identified this protein as one which is involved in carbohydrate building rather than one of the other myriad glycosyltransferases. Furthermore, the enzyme taught by Tavares et al only has 3 amino acid mismatches relative to the instant SEQ ID NO:2 (see sequence alignment provided with the previous Office

Action). Therefore, the property of the specific enzymatic activity claimed would naturally flow from expression of the nucleic acid taught by Tavares et al in a plant.

Allowable Subject Matter

15. Claims 4 and 5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. No claim is allowed.

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHY K. WORLEY whose telephone number is (571)272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00, with additional variable hours before 10:00 and after 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Cathy K. Worley/
Primary Examiner, Art Unit 1638